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RECOGNITION AND MANAGEMENT OF PESTICIDE POISONINGS

U. S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAMS

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AUGUST 1976

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15. Supplementary Notes: This is the new version of the "Clinical Handbook on Pesticide Poisonings".

16. Abstracts: This new treatment manual groups pesticides into major classes such as chlorinated hydrocarbons, chlorophenoxy compounds, arsenicals, etc. Under each major class is listed the general chemical structure, pertinent toxicology related to poisoning, common symptoms, a method for confirmation of diagnosis, and the latest information on management and treatment of pesticide poisonings. The text is aimed mainly at physicians treating patients. However, it will also serve as a valuable reference to those who must evaluate the effects of pesticides on human health and investigators of pesticide accidents will benefit by having information useful to confirm pesticide poisonings.

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pesticide
poisonings
recognition and management of poisonings
solid organochlorines
organophosphate cholinesterase-inhibiting pesticides
carbamate cholinesterase-inhibiting pesticides
Paraquat
Diquat
Morfamquat
Dipyridyls
chlorophenoxy compounds
nitrophenolic herbicides
pentachlorophenol or sodium pentachlorophenate
Urea-, Uracil- and Triazine- based herbicides
acetanilide-,
acetamide-,
carbanilate-,
and anilide-based herbicides
dimethyldithiocarbamate compounds
anticoagulant rodenticides
arsenical pesticides

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PRICES SUBJECT TO CHANGE.

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RECOGNITION AND MANAGEMENT OF PESTICIDE POISONINGS

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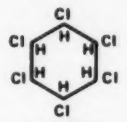
SOLID ORGANOCHLORINE PESTICIDES

CHEMICAL STRUCTURES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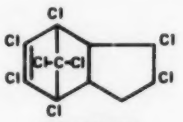
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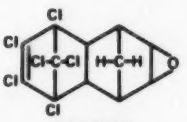
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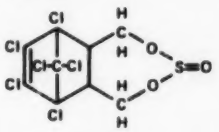
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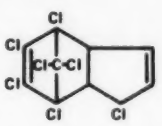
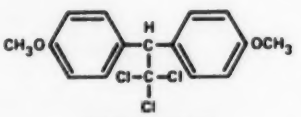

HEPTACHLOR


METHOXYCHLOR

COMMON COMMERCIAL PESTICIDE PRODUCTS (approximately in order of toxicity)

Highly toxic: endrin (Hexadrin), a stereoisomer of dieldrin.

Moderately toxic: aldrin (Aldrite, Drinox), endosulfan (Thiodan), dieldrin (Dieldrite), toxaphene (Toxakil, Strobane-T), lindane (Isotox, Gammexane), benzene hexachloride (BHC, HCH), DDT (Chlorophenothane), heptachlor, kepone, terpene polychlorinates (Strobane), chlordane (Chlordan), dicofol (kelthane), chlorobenzilate (Acaraben), mirex, methoxychlor (Marlate).

TOXICOLOGY

In adequate dosage, these chemicals interfere with axonic transmission of nerve impulses and therefore disrupt the function of the nervous system, principally that of the brain. This results in behavioral changes, sensory and equilibrium disturbances, involuntary muscle activity, and depression of vital centers, particularly that controlling respiration. Adequate doses increase the irritability of the myocardium and cause degenerative changes in the liver.

FREQUENT SYMPTOMS AND SIGNS OF POISONING

APPREHENSION, excitability, dizziness, **HEADACHE, DISORIENTATION,** weakness, **PARESTHESIAE,** muscle twitching, tremor, tonic and clonic **CONVULSIONS** (often epileptiform), coma. Soon after ingestion, nausea and vomiting are often prominent. When chemicals are absorbed by parenteral routes, apprehension, twitching, tremors, and convulsions may be the first symptoms. Respiratory depression is caused by the pesticide and by the petroleum solvents in which these pesticides are usually dissolved. Pallor occurs in moderate to severe poisoning. Cyanosis may result as convulsive activity interferes with respiration.

CONFIRMATION OF DIAGNOSIS

Pesticide and/or metabolites can usually be identified in blood or urine by gas-liquid chromatographic examination of samples taken within 72 hours of poisoning. Some chlorinated hydrocarbon pesticides persist in the serum for weeks or months after absorption. **DO NOT DELAY TREATMENT** of acute poisoning pending confirmatory blood analysis. Presence of chlorinated hydrocarbon residues in blood or tissues does not, of itself, indicate poisoning; actual concentrations are critical to a diagnosis of poisoning.

TREATMENT

1. Establish **CLEAR AIRWAY** and **TISSUE OXYGENATION** by aspiration of secretions, and if necessary, by assisted pulmonary ventilation with oxygen.
2. **CONTROL CONVULSIONS.** The anticonvulsant of choice is **DIAZEPAM (VALIUM). Adult dosage,** including children over 6 years of age or 23 kg in weight: inject 5-10 mgm (1-2 ml) **slowly** intravenously (no faster than one ml per minute), or give total dose intramuscularly (deep). Repeat in 2-4 hours if needed.
   Dosage for children under 6 years or 23 kg in weight: inject 0.1-0.2 mgm/kg (0.02-0.04 ml/kg) **slowly** intravenously (no faster than one-half total dose/minute), or give total dose intramuscularly (deep). Repeat in 2-4 hours if needed.

   CAUTION: Administer intravenous injection slowly to avoid irritation of the vein and occasional hypotension.

   Because of a greater tendency to cause respiratory depression, **BARBITURATES** are probably of less value than **DIAZEPAM.** One used successfully in the past is **PENTOBARBITAL (NEMBUTAL).** Maximum safe dose: 5 mgm/kg body weight, or 0.20 ml/kg body weight, using the usual 2.5% solution.
   If possible, inject solution intravenously, at a rate not exceeding one ml/minute until convulsions are controlled. If intravenous administration is not possible, give total dose rectally, not exceeding 5 mgm/kg body weight (0.2 ml/kg of 2.5% solution).

   CAUTION: Be prepared to assist pulmonary ventilation mechanically if respiration is depressed.

3. If pesticide has been **INGESTED** in quantity sufficient to cause poisoning, the stomach must be emptied.
   If victim is **ALERT** and respiration is not depressed, give **SYRUP OF IPECAC** to induce vomiting (adults and children 12 years and older: 30 ml; children under 12 years: 15 ml).

   CAUTION: OBSERVE THE VICTIM closely after administering **IPECAC.** If consciousness level declines, or if vomiting has not occurred in 15 minutes, proceed immediately to **INTUBATE** the stomach.

Following emesis, have victim drink a suspension of 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to limit absorption of toxicant remaining in the gut.

If the victim is **NOT FULLY ALERT,** empty the stomach immediately by **INTUBATION, ASPIRATION,** and **LAVAGE,** using isotonic saline or 5% sodium bicarbonate. Because many pesticides are dissolved in petroleum distillates, emesis and intubation of the stomach involve a serious risk that solvent will be aspirated, leading to chemical pneumonitis.

For this reason:

A. If the victim is unconscious or obtunded, and if facilities are at hand, insert an **ENDOTRACHEAL TUBE** (cuffed, if available) prior to gastric intubation.

B. Keep the victim's **HEAD BELOW THE LEVEL OF THE STOMACH** during intubation and lavage (Trendelenburg, or left lateral decubitus, with head of table tipped downward). Keep the victim's head turned to the left.

C. **ASPIRATE PHARYNX** as regularly as possible to remove gagged or vomited stomach contents.

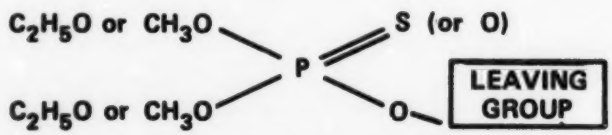
After aspiration of gastric contents and washing of stomach, instill 30 gm of **ACTIVATED CHARCOAL** in 3-4 ounces of water through stomach tube to limit absorption of remaining toxicant. Do **NOT** instill milk, cream, or other substances containing vegetable or animal fats which enhance absorption of chlorinated hydrocarbons.

If bowel movement has not occurred in 4 hours and if patient is fully conscious, give **SODIUM SULFATE** (Glauber's Salts) as a cathartic. (Adults, 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg body weight in 1-6 ounces of water).

4. **BATHE** and **SHAMPOO** the victim vigorously with soap and water if **SKIN** and **HAIR** are contaminated.
5. **DO NOT** give epinephrine or other adrenergic amines, because of the myocardial irritability produced by chlorinated hydrocarbons.
6. During convalescence, enhance **CARBOHYDRATE, PROTEIN,** and **VITAMIN** intake by diet or parenteral therapy to minimize toxic injury to the liver.
7. The chemical **ENDRIN** is much more **HEPATOTOXIC** than are other chlorinated hydrocarbons in common use. Bilirubinemia and elevated blood enzyme activities occur commonly in poisoning. Special measures should be taken to minimize injury by supplying ample nutrients.
8. With the exception of endrin poisoning, the likelihood of recovery from poisoning by most chlorinated hydrocarbon pesticides is generally good, even when convulsions occur. Fatalities occur as a result of massive doses. The prognosis in endrin poisoning is more guarded.

ORGANOPHOSPHATE CHOLINESTERASE-INHIBITING PESTICIDES

GENERAL CHEMICAL STRUCTURE



COMMON COMMERCIAL PESTICIDE PRODUCTS (approximately in order of decreasing toxicity)

Highly toxic: TEPP, phorate (Thimet), mevinphos (Phosdrin), fensulfothion (Dasanit), demeton (Systox), disulfoton (Disyston), sulfotepp (Bladafume, Dithione), Counter, ethyl parathion (Parathion, Thiophos), fonofos (Dyfonate), EPN, azinphosmethyl (Guthion), methyl parathion (Dalf), monocrotophos (Azodrin), dicrotophos (Bidrin), methamidophos (Monitor), carbophenothion (Trithion), phosphamidon (Dimecron).

Moderately toxic: famphur (Warbex, Bo-Ana, Famfos), ethoprop (mocap), coumaphos (Co-Ral), demeton-methyl (Metasystox), dichlorvos (DDVP, Vapona) dioxathion (Delnav), crotoxyphos (Ciodrin), chlorpyrifos (Dursban), ethion, fenthion (Baytex, Entex), diazinon (Spectracide), dimethoate (Cygon), naled (Dibrom), trichlorfon (Dylox, Dipterex, Neguvon), crufomate (Ruelene), ronnel (Korlan), malathion (Cythion). Certain of the organophosphates are systemic, i.e., they are taken up by the plant and translocated into foliage and sometimes into the fruit.

TOXICOLOGY

Toxicants of this class phosphorylate almost irreversibly varying amounts of the acetylcholinesterase enzyme of tissues, allowing accumulation of acetylchloline at cholinergic neuro-effector junctions (muscarinic effects), and at skeletal muscle myoneural junctions and in autonomic ganglia (nicotinic effects). Poison also impairs CNS function. Toxicants can be absorbed by inhalation, ingestion, and skin penetration. Some are converted to more toxic intermediates before they are metabolized. All undergo hydrolytic degradation in liver and other tissues, usually within hours of absorption. Degradation products are of low toxicity, and are excreted in urine and feces.

FREQUENT SYMPTOMS AND SIGNS OF POISONING

Symptoms of acute poisoning develop during exposure or within 12 hours of contact. **HEADACHE, DIZZINESS, EXTREME WEAKNESS, ATAXIA, TINY PUPILS,** blurred or dark vision, muscle **TWITCHING,**

TREMOR, sometimes convulsions, mental confusion, incontinence, unconsciousness. **NAUSEA,** vomiting, abdominal cramps, diarrhea. Tightness in chest, **SLOW HEARTBEAT,** wheezing, productive cough, sometimes **PULMONARY EDEMA** (up to 12 hours after poisoning). **SWEATING,** rhinorrhea, tearing, salivation. Severe poisoning may cause sudden unconsciousness or **TOXIC PSYCHOSIS** resembling acute alcoholism. Extreme **BRADYCARDIA** and heart block have been observed. **RESPIRATORY DEPRESSION** is caused by toxicant and also by hydrocarbon solvent. Continuing absorption at intermediate dosage may cause an **INFLUENZA-LIKE ILLNESS** characterized by weakness, anorexia, and malaise.

CONFIRMATION OF DIAGNOSIS

Depression of plasma and/or RBC cholinesterase activity is the most satisfactory and generally available evidence of excessive absorption of this class of toxicants. Depression of plasma cholinesterase often persists from 1 to 3 weeks; depression of RBC acetylcholinesterase persists up to 12 weeks. Organophosphates yield metabolites that are commonly detectable in the urine of poisoning victims 12 to 48 hours after absorption of significant quantities. The table below lists approximate **LOWER LIMITS OF NORMAL** of plasma and red cell **CHOLINESTERASE ACTIVITIES** of human blood, measured by generally available methods. Test values **BELOW** these levels **usually** indicate excessive absorption of a cholinesterase-inhibiting chemical. (About 3% of individuals have a genetically determined low plasma cholinesterase activity due to generation of an atypical enzyme by the liver.) Whenever possible, comparison of the test sample with a pre-exposure value offers the best confirmation of organophosphate absorption: a depression of 25% or more is strong evidence of excessive absorption.

CAUTION: If diagnosis is probable, do not delay treatment pending confirmation of diagnosis by blood analysis.

TABLE 1. *Approximate Lower Limits of Normal Plasma and Red Cell Cholinesterase Activities in Humans* *

METHOD		PLASMA	RBC	UNITS
ΔpH (Michel)		0.4	0.5	ΔpH per ml per hour
pH STAT (Nabb-Whitfield)		2.3	8.0	μM per ml per hour
ChE-tel (Pfizer)		40		ChE-tel units
A ChE-tel (Pfizer)			210	A ChE-tel units
1-Test Cholinesterase (EM Diagnostics)		3.6		Units per ml
ACHOLEST Test Paper		>20		Minutes
Dupont ACA		<8		Units per ml
Garry-Routh	Male		7.8	
(Micro)	Female		5.8	μM-SH per ml per 3 min
Merckotest			3.0	Units per ml

* Because measurement technique varies among laboratories, more accurate estimates of minimum normal values are usually provided by individual laboratories.

TREATMENT

CAUTION: Persons attending the victim must avoid contamination with vomitus and other sources of toxicant. Wear rubber gloves while decontaminating the victim.

1. Establish **CLEAR AIRWAY** and **TISSUE OXYGENATION** by aspiration of secretions, and if necessary, by assisted pulmonary ventilation with oxygen. Do not administer atropine until a satisfactory level of oxygenation has been achieved. Atropine may induce ventricular fibrillation if victim is severely asphyxic.
2. Administer **ATROPINE SULFATE** intravenously, or intramuscularly if IV injection is not possible. Atropine protects the end-organs from excessive concentrations of acetylcholine. It does not reactivate cholinesterase, and the effects of unmetabolized toxicant may appear as atropinization wears off.

   In **MODERATELY SEVERE** poisoning:

   Adult dosage, including children over 12 years: 0.4-2.0 mgm (1.0 to 5.0 ml of usual 0.4 mgm/ml solution) repeated every 15-30 minutes until atropinization is achieved (tachycardia, flushing, dry mouth, mydriasis). Maintain atropinization by repeated doses for 2-12 hours, depending on severity of poisoning. Watch the patient closely for relapse as atropinization wears off.

   Dosage for children under 12 years: 0.02 mgm/kg body weight (0.05 ml/kg of usual 0.4 mgm/ml solution) repeated every 15-30 minutes until atropinization is achieved.

   In **SEVERE** poisoning, use **TWICE** the dosage of atropine recommended above.
3. Administer **PRALIDOXIME** (Protopam-Ayerst, 2-PAM) in those cases of severe poisoning by **organophosphate** (specifically) pesticides in which muscle weakness and twitchings persist despite atropine therapy. When administered early (less than 36 hours after poisoning) protopam is of value in relieving the nicotinic effects of severe poisoning that are not reversed by atropine.

   Note: Protopam is of no value in poisonings by cholinesterase-inhibiting **carbamate** compounds.

   Adult dose (including children over 12 years): give 1.0 gm intravenously, at no more than 0.5 gm per minute, repeating dose in one hour if muscle weakness has not been relieved.

   Child's dose (under 12 years): give 20-50 mgm per kg (depending on severity) intravenously, injecting no more than half the total dose per minute. This dosage amounts to 0.4 ml-1.0 ml per kg of the recommended 5% solution. Repeat every 10-12 hours as needed, up to 3 times.

   In very severe poisonings, dosage rates may be doubled. Slow administration may be achieved by administering pralidoxime in 250 ml normal saline over a 30-60 minute interval. If intravenous injection is not

possible, pralidoxime may be given by deep intramuscular injection.

CAUTION: Be prepared to assist pulmonary ventilation if respiration is depressed.

4. Observe patient closely at least 24 hours to insure that symptoms (sometimes pulmonary edema) do not occur as atropinization wears off. In very severe poisonings, metabolic disposition of toxicant may require as long as 3 days.
5. **BATHE** and **SHAMPOO** victim with soap and water if there is any chance that **SKIN** and **HAIR** are contaminated.
6. If pesticide has been **INGESTED** in quantity sufficient to cause poisoning, the stomach must be emptied. If victim is alert and respiration is not depressed, give **SYRUP OF IPECAC** to induce vomiting:
   Adults (12 years and over): 30 ml; children under 12 years: 15 ml.

   CAUTION: **OBSERVE** the victim closely after administering **IPECAC.** If consciousness level declines, or if vomiting has not occurred in 15 minutes, proceed immediately to **INTUBATE** the stomach.

   Following emesis, have victim drink a suspension of 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to limit absorption of toxicant remaining in the gut.
   If victim is obtunded or respiration is depressed, empty the stomach by **INTUBATION, ASPIRATION,** and **LAVAGE,** using isotonic saline or 5% sodium bicarbonate. Because many pesticides are dissolved in petroleum distillates, emesis and intubation of the stomach involve a serious risk that solvent will be aspirated, leading to chemical pneumonitis. For this reason:

   A. If the victim is unconscious or obtunded, and if facilities are at hand, insert an **ENDOTRACHEAL TUBE** (cuffed, if available) prior to gastric intubation.
   B. Keep the victim's **HEAD BELOW THE LEVEL OF THE STOMACH** during intubation and lavage (Trendelenburg, or left lateral decubitus, with head of table tipped downward). Keep the victim's head turned to the left.
   C. **ASPIRATE PHARYNX** as regularly as possible to remove gagged or vomited stomach contents.

   After aspiration of gastric contents and washing of stomach, instill 30 gm of **ACTIVATED CHARCOAL** in 3-4 ounces of water through a stomach tube to limit absorption of remaining toxicant.
   If bowel movement has not occurred in 4 hours, and if patient is fully conscious, give **SODIUM SULFATE** (Glauber's Salts) as a cathartic:
   Adults (12 years and older): 15 gm in 6-8 ounces of water.
   Children under 12: 0.2 gm/kg body weight in 1-6 ounces of water.
7. **DO NOT** give morphine, aminophylline, phenothiazines, or reserpine.
8. If intractable **CONVULSIONS** (unresponsive to antidotes) occur in severe poisoning, causes unrelated to direct organophosphate action may

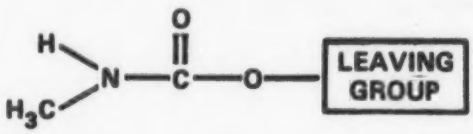
be responsible: head trauma, cerebral anoxia, mixed poisoning. Although not thoroughly tested in these circumstances, **DIAZEPAM** (Valium) (5-10 mgm for adults, 0.1-0.2 mgm/kg for children under 6 years or 23 kg) is probably the safest and most reliable anticonvulsant.

CAUTION: Be prepared to assist pulmonary ventilation mechanically if respiration is depressed, and to counteract hypotensive reactions.

9. Persons who have been clinically poisoned by organophosphate pesticides should not be re-exposed to cholinesterase-inhibiting chemicals until symptoms and signs have resolved completely and blood cholinesterase activities have returned to at least 80% of pre-poisoning values. If blood cholinesterase was not measured prior to poisoning, blood enzyme activities should reach at least minimum normal levels (Table 1) before the victim is returned to a pesticide-contaminated environment.
10. **DO NOT** administer atropine or pralidoxime prophylactically to workers exposed to organophosphate pesticides. It is neither practical nor medically sound to do so.

CARBAMATE CHOLINESTERASE-INHIBITING PESTICIDES

GENERAL CHEMICAL STRUCTURE



COMMON COMMERCIAL PESTICIDE PRODUCTS (approximately in order of toxicity)

Highly toxic: aldicarb (Temik), oxamyl (Vydate), carbofuran (Furadan), methyomyl (lannate, Nudrin), Zectran, methiocarb (Mesurol).

Moderately toxic: propoxur (Baygon), Landrin, carbaryl (Sevin), metalkamate (Bux).

Some chemicals of this class are "systemic," i.e., they are taken up by the plant and translocated into foliage and sometimes into the fruit.

TOXICOLOGY

Toxicants of this class cause reversible carbamylation of the acetylcholinesterase enzyme of tissues, allowing accumulation of acetylcholine at cholinergic neuroeffector junctions (muscarinic effects), and at skeletal muscle myoneural junctions and in autonomic ganglia (nicotinic effects). Poison also impairs CNS function. The carbamyl-enzyme combination dissociates more readily than the phosphorylated enzyme produced by organophosphate insecticides. The lability tends to mitigate the toxicity of carbamates, but also limits the usefulness of blood enzyme measurements in diagnosis of poisoning. Carbamates are absorbed by inhalation, ingestion, and dermal penetration. They are actively metabolized by the liver, and the degradation products are excreted by the liver and kidneys.

A few of the carbamate insecticides are formulated in methyl (wood) alcohol. In cases of ingestion of these formulations, the toxicology of the methanol must be taken fully into consideration: severe gastroenteric irritation, acidosis, and CNS injury.

FREQUENT SYMPTOMS AND SIGNS OF POISONING

Symptoms of acute poisoning develop during exposure or within 12 hours of contact. **HEADACHE, DIZZINESS, WEAKNESS, ATAXIA, TINY PUPILS,** blurred or "dark" vision, muscle **TWITCHING, TREMOR,** sometimes convulsions, mental confusion, incontinence, unconsciousness.

NAUSEA, vomiting, abdominal cramps, diarrhea. Tightness in chest, **SLOW HEARTBEAT,** wheezing, productive cough, occasionally pulmonary edema. Sweating, rhinorrhea, tearing, **SALIVATION.** Severe poisoning may cause sudden unconsciousness, or a toxic psychosis. **RESPIRATORY DEPRESSION** may result from actions of the toxicant and solvent. Continuing absorption at intermediate dosage may cause protracted weakness, anorexia, and malaise.

CONFIRMATION OF DIAGNOSIS

Depression of plasma and/or RBC cholinesterase activity is sometimes useful in detecting excessive absorption of carbamates. However, enzyme activities commonly revert to normal within a few hours. They are not, therefore, reliable detectors of carbamate poisoning; i.e., intoxication may exist when blood cholinesterase activities are normal. The rapid methods for cholinesterase estimation (**ACHOLEST, ChE-TEL, MERCKOTEST**) are more likely to detect depressions. Some carbamates yield metabolites that are measurable in the urine of poisoning victims up to 48 hours after absorption of significant quantities.

The table below lists the approximate **LOWER LIMITS OF NORMAL** plasma and red cell **CHOLINESTERASE ACTIVITIES** of human blood, measured by generally available methods. When test values are **BELOW** these levels, excessive absorption of a cholinesterase-inhibiting carbamate may be suspected. Whenever possible, comparison of the "test" sample with a "pre-exposure" value offers the best confirmation of excessive carbamate absorption: a depression of 25% or more is strong evidence of excessive exposure. (About 3% of individuals have a genetically determined low plasma cholinesterase activity, due to generation of an atypical enzyme by the liver. The red cell acetylcholinesterase is normal in these cases.)

TABLE 1. *Approximate Lower Limits of Normal Plasma and Red Cell Cholinesterase Activities in Humans* *

METHOD		PLASMA	RBC	UNITS
ΔpH (Michel)		0.4	0.5	ΔpH per ml per hour
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ChE-tel (Pfizer)		40		ChE-tel units
A ChE-tel (Pfizer)			210	A ChE-tel units
1-Test Cholinesterase (EM Diagnostics)		3.6		Units per ml
ACHOLEST Test Paper		>20		Minutes
Dupont ACA		<8		Units per ml
Garry-Routh	Male		7.8	
(Micro)	Female		5.8	μM-SH per ml per 3 min
Merckotest			3.0	Units per ml

* Because measurement technique varies among laboratories, more accurate estimates of minimum normal values are usually provided by individual laboratories.

CAUTION: If diagnosis is probable, do not delay treatment pending confirmation of diagnosis by blood analysis.

TREATMENT

CAUTION: Persons attending the victim must avoid contamination with vomitus and other sources of toxicant. Wear rubber gloves while decontaminating the victim.

1. Establish **CLEAR AIRWAY** and **TISSUE OXYGENATION** by aspiration of secretions, and if necessary, by assisted pulmonary ventilation with oxygen. Do not administer atropine until a satisfactory level of oxygenation has been achieved. Atropine may induce ventricular fibrillation if the victim is severely asphyxic.
2. Administer **ATROPINE SULFATE** intravenously, or intramuscularly if IV injection is not possible. Atropine protects the end-organs from excessive concentrations of acetylcholine. It does not reactivate cholinesterase, and effects of unmetabolized toxicant may appear as atropinization wears off.
   In **MODERATELY SEVERE** poisoning:
   Adult dose (including children over 12 years): 0.4-2.0 mg/kg body weight (1.0-5.0 ml of usual 0.4 mgm/ml solution) repeated every 15-30 minutes until atropinization is achieved (tachycardia, flushing, dry mouth, mydriasis). Maintain atropinization by repeated doses for 2-12 hours, depending on severity of poisoning.
   Child's dose: 0.01 mgm/kg body weight (0.05 ml/kg of usual 0.4 mgm/ml solution) repeated every 15-30 minutes until atropinization is achieved. In **SEVERE** poisoning: use **TWICE** the dosage of atropine recommended above.
3. Do **NOT** give pralidoxime Protopam-Ayerst, 2-PAM). It is of no value in carbamate poisonings.
4. **OBSERVE** patient closely at least **24 HOURS** to insure that symptoms (possibly pulmonary edema) do not occur as atropinization wears off.
5. **BATHE** and **SHAMPOO** victim with soap and water if there is any chance that **SKIN** and **HAIR** are contaminated.
6. If pesticide has been **INGESTED,** the stomach must be emptied. If victim is alert and respiration is not depressed, give **SYRUP OF IPECAC** to induce vomiting: adults (including children over 12), 30 ml; children under 12, 15 ml.

   CAUTION: **OBSERVE** the victim closely after administering **IPECAC.** If consciousness level declines, or if vomiting has not occurred in 15 minutes, proceed immediately to **INTUBATE** the stomach.

   Following emesis, have victim drink a suspension of 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to bind toxicant remaining in the gastrointestinal tract.
   If victim is obtunded or respiration is depressed, empty the stomach by

INTUBATION, ASPIRATION, and **LAVAGE,** using isotonic saline of 5% sodium bicarbonate. Because many pesticides are dissolved in petroleum distillates, emesis and intubation of the stomach involve a serious risk that solvent will be aspirated, leading to chemical pneumonitis. For this reason:

A. If the victim is unconscious or obtunded, and if facilities are at hand, insert an **ENDOTRACHEAL TUBE** (cuffed, if available) prior to gastric intubation.

B. Keep the victim's **HEAD BELOW THE LEVEL OF THE STOMACH** during intubation and lavage (Trendelenburg, or left lateral decubitus, with head of table tipped downward). Keep the victim's head turned to the left.

C. **ASPIRATE PHARYNX** as regularly as possible to remove gagged or vomited stomach contents.

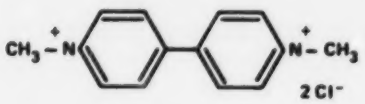
After aspiration of gastric contents and washing of stomach, instill 30 gm of **ACTIVATED CHARCOAL** in 3-4 ounces of water through a tube to limit absorption of remaining toxicant.

If bowel movement has not occurred in 4 hours, and if patient is fully conscious, give **SODIUM SULFATE** as a cathartic. Adult dose, including children over 12: 15 gm in 6-8 ounces of water. For children under 12, give 0.2 gm/kg body weight in 1-6 ounces of water.

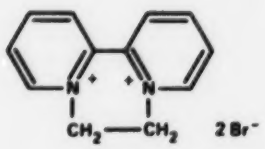
7. **DO NOT** give morphine, aminophylline, phenothiazines, or reserpine.
8. **CONVULSIONS** are uncommon manifestations of poisoning by carbamates. If they occur, causes other than direct carbamate action should be considered: cerebral anoxia, head trauma, mixed poisoning. Although not tested in these circumstances, **DIAZEPAM** (Valium) is probably the anticonvulsant of choice. Dosage for adults and children over 6 years or 23 kg body weight is 5-10 mgm given **slowly** IV (no more than half total dose per minute, or intramuscularly, (deep). Dosage for children under 6 years, or 23 kg body weight, is 0.1-0.2 mgm/kg. Repeat this dosage every 2-4 hours if needed to control convulsions. Be prepared to intubate and to assist pulmonary ventilation mechanically if respiration is depressed. Hypotensive reactions may also occur.
9. Persons who have been clinically poisoned by carbamate pesticides should not be re-exposed to cholinesterase-inhibiting chemicals until symptoms and signs have resolved completely and blood cholinesterase activities have returned to at least 80% of pre-poisoned values. If blood cholinesterase was not measured prior to poisoning, blood enzyme activities should reach at least minimum normal levels (Table 1) before the victim is returned to a pesticide-contaminated environment.
10. Do **NOT** administer atropine prophylactically to workers exposed to carbamate insecticides. It is neither practical nor medically sound to do so.

PARAQUAT, DIQUAT, AND MORFAMQUAT (Dipyridyls)

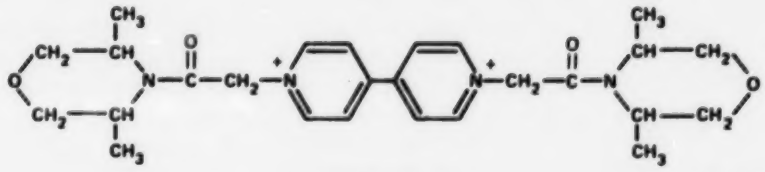
CHEMICAL STRUCTURES



PARAQUAT



DIQUAT



MORFAMQUAT 2 Cl⁻

COMMON COMMERCIAL PESTICIDE PRODUCTS

The highly polar dipyridyl compounds are available commercially as halide and dimethyl sulfate salt solutions. Both are used as contact herbicides; diquat is particularly effective against water weeds. Plant tissues and soil particles adsorb dipyridyl compounds strongly. Concentrates are more likely to cause poisoning than are the more dilute agents sold over the counter.

Paraquat products: Paraquat Cl, Dual Paraquat, EM-7217, Gramoxone S, Weedol and Dextrone X are all concentrates containing 20% paraquat ion. Preeglone extra and Gramonol are concentrate mixtures with other herbicides. Ortho Spot Weed and Grass Killer contains 0.2% paraquat ion.

Diquat products: Aquakill, Aquacide, Heavy Duty Weed Control, Aquatate, Aquatic Weed Killer, Reglone, Vegetrole, Watrol, and Di-Kill Vegetation Killer are all packaged as concentrates. Preeglone extra is a concentrate mixture with paraquat.

Morfamquat products: Morfoxone, PP-745.

TOXICOLOGY

The dipyridyl compounds bind to, and injure, the epithelial tissues of the skin, nails, eyes, nose, mouth, and respiratory and gastrointestinal tracts. Concentrated solutions cause inflammation and sometimes necrosis and ulceration of mucosal linings.

The toxicology of paraquat has been more thoroughly investigated than

that of the other dipyridyls. Diquat appears to be substantially less toxic than paraquat. Little is known of the effects of morfamquat.

The consequences of **ingestion of paraquat concentrate** (which accounts for nearly all of the mortality and serious morbidity from these compounds) are unique. Because dosages necessary to produce poisoning in humans vary widely, all cases of ingestion should be treated vigorously, regardless of estimated intake.

For 24-72 hours, there is often very little indication of systemic toxicity. Evidence of poisoning may be limited to pain, vomiting, and diarrhea from irritation of the gastrointestinal linings. At 48 to 72 hours, kidney damage may be apparent from proteinuria, hematuria, and rising BUN and creatinine levels. Liver damage is reflected in hyperbilirubinemia, often associated with increased serum GOT, GPT, alkaline phosphatase, and LDH enzyme activities. From 72 hours to as long as 14 days after ingestion, indications of a diffuse toxic pneumonitis often appear.

Histopathology of the pulmonary lesion is complex, commencing with intra-alveolar edema and hemorrhage, then rapid proliferation of bronchiolar epithelium and fibrous connective tissue. Focal atelectasis occurs, possibly as a result of impaired synthesis of pulmonary surfactant. The functional consequence is impaired gas exchange, due to patchy consolidation, alveolar collapse and increased airway resistance. The proliferation of fibrous connective tissue is often progressive, and so generalized as to cause death in 1-3 weeks. Surviving patients should be examined for evidence of residual fibrosis up to 6 months after poisoning. Injuries to liver and kidney are commonly reversible, ameliorating even as the pulmonary lesion worsens.

Electrocardiographic evidence of toxic myocarditis is commonly observed, and cranial nerve palsies have been reported as toxic manifestations.

Lens cataracts have been reported in laboratory animals given diquat by mouth.

FREQUENT SYMPTOMS AND SIGNS OF POISONING

Skin **IRRITATION,** drying, and cracking follow untreated skin contact with paraquat. **DISCOLORATION** and **IRREGULARITY** of **FINGERNAILS** commonly occur in workers regularly exposed to paraquat concentrates. Delayed **CONJUNCTIVITIS** and **KERATITIS** develop 12-48 hours after contact with the eye. Inhalation of spray droplets irritates the nose and throat, and sometimes causes **NOSEBLEED.**

FOLLOWING INGESTION of paraquat concentrate, the earliest symptoms and signs are due to mucosal irritation and ulceration of the gastrointestinal tract. **PAIN** (oral, substernal, abdominal), **VOMITING,** and **DIARRHEA** (sometimes melena) occur. Generalized **MUSCLE ACHING** is reported. Early symptoms are sometimes so mild that vigorous treatment is improperly delayed.

From 48-72 hours, indications of renal and hepatic insult appear. Albuminuria, hematuria, pyuria, and elevated BUN and creatinine occur. **OLIGURIA** may develop, and this signals severe poisoning. **JAUNDICE** and

elevations of serum GOT, GPT, alkaline phosphatase and LDH reflect hepatocellular injury. The effects on liver and kidney are generally reversible. Indications of lung injury usually appear 72-96 hours after exposure, but may be delayed as long as 14 days. **COUGH, DYSPNEA,** and **TACHYPNEA** often progress in the manner of a diffuse pneumonitis. In some cases, severe **PULMONARY EDEMA** occurs and persists for several days. The lung disease usually progresses to death.

CONFIRMATION OF DIAGNOSIS

Qualitative and quantitative methods for paraquat and diquat in urine are available at some toxicology laboratories and at the Chevron Environmental Health Center, 225 Bush Street, San Francisco, California 94104, telephone (415) 233-3737.

TREATMENT

1. Contaminated **SKIN** must be **FLUSHED** with copious amounts of water. Material splashed in the **EYES** must be removed by **PROLONGED IRRIGATION** with clean water. Eye contamination should thereafter be treated by an ophthalmologist.
2. **INGESTION** of **ANY DIPYRIDYL** should be treated promptly and vigorously to **LIMIT ABSORPTION** from the gastrointestinal tract and **ACCELERATE EXCRETION** of material already absorbed. Because the absorption of dipyridyls from the gut is relatively slow, measures to **MINIMIZE ABSORPTION** offer the most promising opportunity to save the victim. **These measures must be undertaken even though the patient is essentially free of signs of systemic toxicity, and even when, by all accounts, the ingested dose was probably small and was taken as long as 72 hours before treatment.**
   A. **LAVAGE THE STOMACH** with at least 2 liters normal saline or 5% sodium bicarbonate solution. With stomach tube still in place, introduce a slurry of 8-10 ounces of **ADSORBENT,** allowing as much time as necessary for the material to be accommodated without overdistension of the stomach. Suitable adsorbents are, in order of effectiveness: Fuller's Earth *, 30% suspension, and bentonite (or Montmorillonite), 7% suspension. These agents effectively bind

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* Optimal mesh 100-200. Sources of adsorbents are as follows:
  Sigma Chemical Company, 3500 Dekalb Street, St. Louis, Missouri 63178
  Robinson's Bentonite U.S.P., Cat. No. 1138, Robinson Laboratories, Inc., San Francisco, California 94104
  Robinson's Fuller's Earth U.S.P., Cat. No. 1343, Robinson Laboratories, Inc., San Francisco, California 94104
  U.S.P. Volclay Bentonite, American Colloid Company, Skokie, Illinois
  Emathlite VMP 600, Mid-Florida Mining Co., Lowell, Florida 32663

dipyridyls with which they come in contact in vivo. Activated charcoal is less effective, but should be used if other agents are not immediately available. Allow about one hour for the adsorbent to contact the toxicant before administering **SODIUM SULFATE** as a cathartic (adults, 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg body weight in 1-6 ounces of water). Repeat dosage of Fuller's Earth (or other adsorbent if Fuller's Earth is not available) by mouth every 4 hours for at least 12 complete doses. Repeat saline catharsis if continuing bowel movements do not occur.

B. Institute a regimen of **FORCED DIURESIS.** Put a retention catheter in place to insure accurate monitoring of urine output. Inquire into possible medical limitations to the victim's ability to tolerate high fluid loads. Examine the urine sediment to assess likelihood that dipyridyl injury to the kidneys has already reduced tolerance to fluid infusion by severe tubular injury.

In the absence of contraindications, **INFUSE** intravenously, in rotation, solutions of either glucose, electrolyte or mannitol. As time progresses, particular electrolyte solutions will be required to maintain normal extracellular fluid composition.

Give parenteral **FUROSEMIDE** (Lasix) by slow intravenous injection to sustain diuresis. Adult dose: 20-40 mgm every 2-6 hours.

MONITOR FLUID BALANCE AND BLOOD ELECTROLYTE CONCENTRATIONS regularly and look for signs of fluid overload (basilar rales, venous distension, high central venous pressure) that would warn of excessive fluid accumulation.

If circumstances do not permit vigorous forced diuresis undertake **PERITONEAL DIALYSIS** or **EXTRACORPOREAL HEMODIALYSIS.** These measures appear to offer little advantage over forced diuresis in victims able to tolerate high rates of intravenous fluid infusion. Hemodialysis with ultrafiltration is reported to offer effective removal of paraquat from the circulating blood.

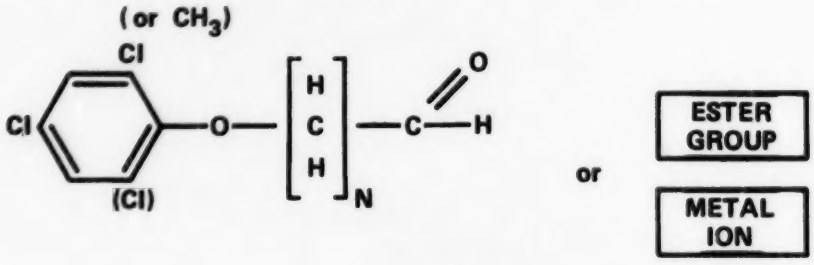
Measure dipyridyl in urine to estimate levels of remaining toxicant.

3. **DO NOT ADMINISTER SUPPLEMENTAL OXYGEN,** unless arterial pO_2 drops below 60-70 mm Hg. Increased levels of alveolar oxygen accelerate the pathologic process caused by dipyridyls.
4. **SUPEROXIDE DISMUTASE** (Truett Laboratories) is an enzyme from bovine erythrocytes which, by virtue of its free radical scavenging property, represents a rational antidote for dipyridyl poisoning. Tests of antidotal power in rats have yielded very promising results. The value of the material in treating human poisonings has not yet been reported. It can be given both by aerosol and intravenously, and appears to be nontoxic.
5. Corticosteroids have usually been administered in human poisoning cases. While they have not influenced the outcome adversely, neither have they proven definitely beneficial. Immunosuppressive drugs have been tried in a few cases without apparent benefit.

6. There is some evidence that expectorants (especially ammonium chloride and potassium iodide) may be of therapeutic value in minimizing the reduction in lung surfactant activity that is characteristic of paraquat poisoning.

CHLOROPHENOXY COMPOUNDS

GENERAL CHEMICAL STRUCTURE



COMMON COMMERCIAL PESTICIDE PRODUCTS

2,4-D (Weedone), 2,4,5-T 2,4,5-TP, Silvex (Kuron), 2,4-DB (Butyrac, Butoxone), erbon, Fenac, 2,4-DEP, MCPA, MCPB, MCPP (Mecoprop), Weedestron, Esteron, Estone, Dacamine, Weed-B-Gon, Weed-No-More, Weed-Out, Ded-Weed, Weed or Brush-Rhap, Broadleaf Weed Killer, Dandelion Killer, Vegetation Killer, Chickweed and Clover Killer. Several hundred herbicide preparations include one or more **CHLOROPHENOXY COMPOUND.** They can usually be identified in the active ingredient description on the product label.

TOXICOLOGY

The chlorophenoxy acids, salts, and esters are mildly to severely irritating to skin, eyes, and respiratory and gastrointestinal linings. They are absorbed across the gut wall, the lung, and the skin. They are not significantly fat storable: excretion occurs within hours, or at most days, primarily in the urine.

These compounds apparently have very low toxic potential for most individuals. Human subjects have tolerated 0.5 gm ingested doses daily for 2-4 weeks without adverse effects. Paradoxically, several cases of peripheral neuropathy have been reported in workers after seemingly minor exposures to 2,4-D. Whether these individuals were peculiarly predisposed, or were exposed concurrently to other unidentified neurotoxic materials, is not known. In a few individuals, local depigmentation has apparently resulted from prolonged and repeated dermal contact with chlorophenoxy materials.

Given in large doses to experimental animals, 2,4-D causes vomiting, diarrhea, anorexia, weight loss, ulcers of the mouth and pharynx, and toxic injury to the liver, kidneys, and central nervous system. Myotonia (stiffness and incoordination of hind extremities) develops in some species and is apparently due to CNS damage: demyelination has been observed in the dorsal columns of the cord, and EEG changes have indicated functional disturbances in the brains of heavily dosed experimental animals. A single victim of acci-

dental ingestion of over 7 gm of 2,4-D exhibited direct toxic damage to skeletal muscle, manifest as myoglobinuria and creatinuria. Other chemicals in the ingested formulation may have contributed to the unusual pathology in this case. In another isolated instance of extreme dosage, convulsions apparently occurred before death.

FREQUENT SYMPTOMS AND SIGNS OF INJURY AND POISONING

IRRITATION of the skin follows excessive contact with many chlorophenoxy compounds. Prolonged inhalation of spray is likely to irritate the nose, eyes, throat and bronchi, causing disagreeable local **BURNING SENSATIONS** and **COUGH.** Prolonged inhalation has also caused **DIZZINESS** and **ATAXIA,** usually of a transient nature. **WHEN INGESTED,** these compounds **IRRITATE** the **MOUTH** and **THROAT,** and usually cause enough gastrointestinal irritation to induce prompt **EMESIS. CHEST PAIN** from esophagitis is common. **ABDOMINAL PAIN** and **TENDERNESS** and **DIARRHEA** usually ensue. Absorption of large quantities of chlorophenoxy herbicide may produce **FIBRILLARY MUSCLE TWITCHING, SKELETAL MUSCLE TENDERNESS,** and **MYOTONIA** (stiffness of muscles of extremities). Respiratory insufficiency from muscle weakness apparently occurred in one victim of accidental poisoning, although poisoning in this case may have involved additional toxicants.

CONFIRMATION OF DIAGNOSIS

Gas-liquid chromatographic methods are available for detecting and measuring many of the chlorophenoxy compounds in urine. These analyses are useful in confirming and assessing the magnitude of toxicant absorption. Urine samples should be collected as soon as possible after exposure because the herbicides may be almost completely excreted in 24-72 hours, depending on the dose. Analyses can be performed at special laboratories operated by States, agricultural research facilities, commercial chemical companies, and the U.S. Environmental Protection Agency.

Treatment should not be delayed pending confirmation of the causative agent, if there is a strong circumstantial basis for the diagnosis.

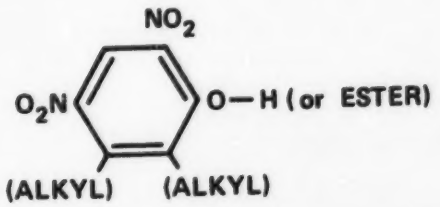
TREATMENT

1. **BATHE** and **SHAMPOO** with soap and water to remove chemicals from the skin and hair. Individuals with chronic skin disease or known sensitivity to chemicals should either avoid using these herbicides or should take extraordinary measures to avoid direct contact.
2. **FLUSH** contaminating chemicals from the eyes with copious amounts of clean water for 10-15 minutes.
3. If symptoms of illness occur during or following inhalation of spray, **REMOVE** the victim **FROM CONTACT** with the material for at least 2 days. Allow subsequent use of chlorophenoxy compounds only if effective respiratory protection is practiced.

4. When chemicals of this class have been **INGESTED,** spontaneous emesis usually occurs, and may empty the stomach as effectively as intubation and lavage. If vigorous emesis has not occurred, and **IF VICTIM IS FULLY ALERT,** induce **EMESIS** with **SYRUP** of **IPECAC** (adults 12 years and older, 30 ml; children under 12 years, 15 ml).
   A. If consciousness level is depressed, an effect of the solvent petroleum distillates and/or other pesticides should be suspected. In this case, empty the stomach by **INTUBATION, ASPIRATION, AND LAVAGE,** using all available means to avoid aspiration of vomitus: Trendelenberg or left lateral decubitus position, frequent aspiration of the pharynx, and in unconscious victims, tracheal intubation (using a cuffed tube), prior to gastric intubation.
   B. After emesis or aspiration of the stomach and washing with isotonic saline or sodium bicarbonate, administer or instill 30 gm of **ACTIVATED CHARCOAL** in 3-4 ounces of water to limit absorption of remaining toxicant.
   C. If the irritant properties of the toxicant fail to produce a bowel movement in 4 hours, and if the patient is fully conscious, give **SODIUM SULFATE** (Glauber's Salts) as a cathartic (adults 12 years and older, 15 gm in 6-8 ounces of water; children under 12, 0.2 gm/kg of body weight in 1-6 ounces of water).
   D. If absorption of as much as 0.5 gm may have occurred in an adult (or about 0.02 gm/kg in children under 12 years), administer glucose and electrolyte solution intravenously to accelerate excretion of toxicant. Observe the patient for renal irritation (albuminuria, hematuria); liver injury (serum bilirubin, alkaline phosphatase, serum LDH, GOT and GPT); gastrointestinal ulceration (melena); leukopenia (WBC and differential); myalgia and myotonia (manifest as stiffness and incoordination); and peripheral neuropathy (paresthesiae, pain, hypesthesia and paresis of the extremities).

NITROPHENOLIC HERBICIDES

GENERAL CHEMICAL STRUCTURE



COMMON COMMERICIAL PESTICIDE PRODUCTS

Dinitrophenol (Chemox PE), dinitroorthocresol (DNOC, DNC, Sinox), Dinoseb (DNBP, DN-289), dinosam (DNAP), DN-111 (DNOCHP), dinoprop, dinoterbon, dinoterb, dinosulfon, binapacryl (Morocide, Endosan, Ambox, Mildex), dinobuton, dinopenton.

TOXICOLOGY

These materials should be regarded as highly toxic to humans and animals. Most nitrophenols and nitrocresols are well absorbed from the gastrointestinal tract, across the skin, and by the lung when very fine droplets are inhaled. Except in a few sensitive individuals, they are only moderately irritating to the skin. They usually produce a yellow stain wherever contact occurs. Like other phenols, they are toxic to the liver, kidney, and nervous system. Basic mechanism of toxicity is a stimulation of oxidative metabolism in cell mitochondria, by interference with the normal coupling of carbohydrate oxidation to phosphorylation reactions. Increased oxidative metabolism depletes body carbohydrate and fat stores and leads to pyrexia, tachycardia, and dehydration. Most severe poisonings from absorption of these compounds have occurred in workers who were concurrently exposed to hot environments. Direct action on the brain causes cerebral edema, manifest clinically as a toxic psychosis and sometimes as convulsions. Liver parenchyma and renal tubules show degenerative changes. Albuminuria, pyuria, hematuria, and increased BUN are often prominent signs of renal injury. Agranulocytosis has occurred following large doses of dinitrophenol.

Cataracts have occurred in some chronically poisoned laboratory species. This is a possible, but as yet unconfirmed, hazard in humans.

Death in nitrophenol poisoning is followed promptly by intense rigor mortis.

FREQUENT SYMPTOMS AND SIGNS OF POISONING

YELLOW STAINING of skin and hair signify contact with a nitrophenolic chemical. Staining of the sclerae and urine indicate absorption of potentially

toxic amounts. **PROFUSE SWEATING, HEADACHE, THIRST, MALAISE,** and **LASSITUDE** are the common early symptoms of poisoning. **WARM, FLUSHED, SKIN, TACHYCARDIA,** and **FEVER** characterize a serious degree of poisoning. **APPREHENSION,** restlessness, anxiety, manic behavior, or unconsciousness reflect severe cerebral injury. Cyanosis, tachypnea and dyspnea occur as a consequence of extreme stimulation of metabolism, pyrexia, and tissue anoxia. Weight loss occurs in persons chronically poisoned at low dosages.

CONFIRMATION OF DIAGNOSIS

Unmetabolized nitrophenols and nitrocresols can be identified spectrophotometrically in the serum and urine at concentrations well below those necessary to cause poisoning. Many laboratories can also analyze for these compounds by gas-liquid chromatography. If poisoning is probable, do not await confirmation before commencing treatment.

TREATMENT

1. **WASH** contaminated **SKIN** and **HAIR** promptly with soap and water.
2. **FLUSH** chemical from **EYES** with copious amounts of clean water.
3. **IN EVENT OF SYSTEMIC POISONING:**
   - A. **REDUCE BODY TEMPERATURE BY PHYSICAL MEANS.** Sponge baths and low-temperature blankets probably offer the best opportunity for survival of poisonings by these agents. In fully conscious patients, administer cold, sugar-containing liquids by mouth, as tolerated.
   - B. Administer **OXYGEN** continuously by mask to minimize tissue anoxia.
   - C. Administer **INTRAVENOUS FLUIDS** at maximum tolerated rates to enhance urinary excretion of toxicant and to support physiologic mechanisms for heat loss. Monitor blood electrolytes and sugar, adjusting IV infusions to stabilize electrolyte concentrations.
   - D. Administer **SEDATIVES** if necessary to control apprehension and excitement. Amobarbital or **PENTOBARBITAL,** 100-200 mgm IM or slowly IV, every 4-6 hours, may be needed in adults (child's dose: up 5 mgm/kg body weight). Although not previously used in this type of poisoning, **DIAZEPAM** (Valium) should be of value: adult dose 5-10 mgm intramuscularly, or **slowly** IV, dosage for children under 6 years or 23 kg: 0.1-0.2 mgm/kg. Repeat every 2-4 hours as needed.

     CAUTION: Be prepared to counteract respiratory depression and hypotension, which may occur following administration of anticonvulsants.
   - E. If toxicant has been **INGESTED,** the stomach must be emptied. If victim is alert and respiration is not depressed, give **SYRUP OF IPECAC** to induce vomiting (adults 12 years and older: 30 ml;

children under 12: 15 ml).

CAUTION: OBSERVE the victim closely **AFTER** administering **IPECAC.** If consciousness level declines, or if vomiting has not occurred in 15 minutes, proceed immediately to **INTUBATE** and **LAVAGE** the stomach.

Following emesis, have victim drink a suspension of 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to bind toxicant remaining in the gastrointestinal tract.

IF VICTIM IS NOT FULLY ALERT, empty the stomach immediately by **INTUBATION, ASPIRATION,** and **LAVAGE,** using isotonic saline or 5% sodium bicarbonate. Because these pesticides are usually dissolved in petroleum distillates, emesis and intubation of the stomach involve a serious risk that solvent will be aspirated, leading to chemical pneumonitis. For this reason:

(1) If the victim is unconscious or obtunded, and if facilities are at hand, insert an **ENDOTRACHEAL TUBE** (cuffed, if available) prior to gastric intubation.

(2) Keep the victim's **HEAD BELOW THE LEVEL OF THE STOMACH** during intubation and lavage (Trendelenburg, or left lateral decubitus, with head of table tipped downward). Keep the victim's head turned to the left.

(3) **ASPIRATE PHARYNX** as regularly as possible to remove gagged or vomited stomach contents.

After aspiration of gastric contents and washing of stomach, instill 30 gm of **ACTIVATED CHARCOAL** in 3-4 ounces of water through the stomach tube to limit absorption of remaining toxicant. Do **NOT** instill milk, cream or other materials containing vegetable or animal fats, as these are likely to enhance absorption.

If bowel movement has not occurred in 4 hours, and if patient is fully conscious, give **SODIUM SULFATE** (Glauber's Salts) as a cathartic (adults 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg body weight in 1-6 ounces of water).

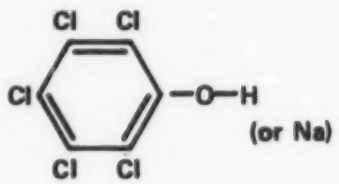
F. **DO NOT** administer aspirin or other antipyretics to control fever. Animal tests indicate that aspirin enhances, rather than reduces, the toxicity of nitrophenolic and nitrocresolic compounds.

G. During convalescence, administer high-calorie, high-vitamin diet to facilitate repletion of body fat and carbohydrate stores.

H. Discourage subsequent contact with the toxicant for at least 4 weeks, to allow full restoration of normal metabolic processes.

PENTACHLOROPHENOL OR SODIUM PENTACHLOROPHENATE

CHEMICAL STRUCTURE



COMMON COMMERCIAL PESTICIDE PRODUCTS

PCP, Dowicide-7, Penchlorol, Pentacon, Penwar, Weedone, Veg-I-Kill, Wood Preserver, Wood Tox 140, Purina Insect Oil Concentrate, Gordon Termi Tox, Usol Cabin Oil, Certified Kiltrol-74 Weed Killer, Ciba-Geigy Ontrack OS 3, 4 or 5, Ortho Triox Liquid Vegetation Killer, Black Leaf Grass. Weed and Vegetation Killer Spray.

Pentachlorophenol has many uses as a weed killer, defoliant, wood preservative, germicide, fungicide, and molluscicide. It is an ingredient of many other formulated mixtures sold for one or more of these purposes.

TOXICOLOGY

Pentachlorophenol irritates the skin, eyes, and upper respiratory mucous membranes. It is efficiently absorbed across the skin, the lung, and the gastrointestinal lining. Like the nitrophenolic compounds, it stimulates oxidative metabolism of tissue cells by uncoupling oxidative processes from the normal stepwise phosphorylation reactions. In common with other phenols, it is toxic to the liver, kidney, and central nervous system. Impurities in the technical formulation may well be responsible for chloracne.

The majority of severe poisonings have occurred in workers exposed to hot environments. However, a major epidemic of poisoning occurred in newborn infants who absorbed PCP from treated diapers. Dehydration and metabolic acidosis are important features of poisoning in children.

Albuminuria, glycosuria, and elevated BUN reflect renal injury. Liver enlargement has been observed in some cases. Anemia and leukopenia have been found in chronically exposed workers, but leucocytosis is more commonly found in acute poisoning.

FREQUENT SYMPTOMS AND SIGNS OF POISONING

IRRITATION of nose, throat, eyes, and skin is the most common symptom of exposure to PCP. Severe or protracted exposure may result in a **CONTACT DERMATITIS.** Intensive occupational exposure has resulted in chloracne.

PROFUSE SWEATING, HEADACHE, WEAKNESS, and **NAUSEA** are the most consistent presenting symptoms of systemic poisoning by absorbed PCP. **FEVER** is usually present but may be minimal or absent. **TACHYCARDIA, TACHYPNEA,** and **PAIN** in the **CHEST** and **ABDOMEN** are often prominent. **THIRST** is usually intense, but may be masked by nausea and vomiting. **DECLINING MENTAL ALERTNESS** may progress to stupor and/or convulsions. Protracted exposure results in **WEIGHT LOSS** from increased basal metabolic rate.

CONFIRMATION OF DIAGNOSIS

PCP can be measured in blood, urine, and adipose tissue by gas-liquid chromatography. A few parts per **billion** can usually be found in the blood and urine of persons having no known exposure. Based on studies of persons occupationally exposed to PCP, symptoms of systemic toxicity probably do not appear in adults until blood and urine concentrations reach at least one part per million (0.1 mgm %, or 1,000 parts per billion).

If poisoning is strongly suspected on grounds of exposure history, symptoms and signs, do not postpone treatment until diagnosis is confirmed.

TREATMENT

1. **BATHE** and **SHAMPOO** contaminated **SKIN** and **HAIR** promptly with soap and water.
2. **FLUSH** chemical from **EYES** with copious amounts of clean water.
3. **IN EVENT OF SYSTEMIC POISONING**
   A. **REDUCE BODY TEMPERATURE BY PHYSICAL MEANS.** Sponge baths and low-temperature blankets probably offer the best opportunity for survival of poisonings by these agents. In fully conscious patients, administer cold, sugar-containing liquids by mouth, as tolerated.
   B. Administer **OXYGEN** continuously by mask to minimize tissue anoxia.
   C. Administer **INTRAVENOUS FLUIDS** at maximum tolerated rates to enhance urinary excretion of toxicant and to support physiologic mechanisms for heat loss. Monitor blood electrolytes and sugar, adjusting IV infusions to stabilize electrolyte concentrations.
   D. Administer **SEDATIVES** if necessary to control apprehension and excitement. Amobarbital or pentobarbital, 100-200 mgm IM or slowly IV, every 4-6 hours may be needed. (Children's dosage: 5 mgm/kg.) Diazepam, 10 mgm intramuscularly, should be valuable, although its use has not been reported in this type of poisoning. (Children's dosage: 0.1-0.2 mgm/kg.)

   CAUTION: Be prepared to assist pulmonary ventilation mechanically in event of respiratory depression, and to counteract any hypotensive reaction.

E. If toxicant has been **INGESTED,** the stomach must be emptied. If victim is alert and respiration is not depressed, give **SYRUP OF IPECAC** to induce vomiting. (Adults, 12 years and older: 30 ml; children under 12: 15 ml.)

CAUTION: **OBSERVE** the victim closely **AFTER** administering **IPECAC.** If consciousness level declines, or if vomiting has not occurred in 15 minutes, proceed immediately to **INTUBATE** the stomach.

Following emesis, have victim drink a suspension of 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to bind toxicant remaining in the gastrointestinal tract.

If victim is not fully alert, empty the stomach immediately by **INTUBATION, ASPIRATION,** and **LAVAGE,** using isotonic saline or 5% sodium bicarbonate. Because these pesticides are usually dissolved in petroleum distillates, emesis and intubation of the stomach involve a serious risk that solvent will be aspirated, leading to chemical pneumonitis. For this reason:

(1) If the victim is unconscious or obtunded, and if facilities are at hand, insert an **ENDOTRACHEAL TUBE** (cuffed, if available) prior to gastric intubation.

(2) Keep the victim's **HEAD BELOW THE LEVEL OF THE STOMACH** during intubation and lavage (Trendelenburg, or left lateral decubitus, with head of table tipped downward). Keep the victim's head turned to the left.

(3) **ASPIRATE PHARYNX** as regularly as possible to remove gagged or vomited stomach contents.

After aspiration of gastric contents and washing of stomach, instill 30 gm of **ACTIVATED CHARCOAL** in 3-4 ounces of water through a stomach tube to limit absorption of remaining toxicant. Do **NOT** instill milk, cream, or other materials containing vegetable or animal fats which are likely to enhance absorption.

If bowel movement has not occurred in 4 hours, and if patient is fully conscious, give **SODIUM SULFATE** (Glauber's Salts) as a cathartic (adults 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg body weight in 1-6 ounces of water).

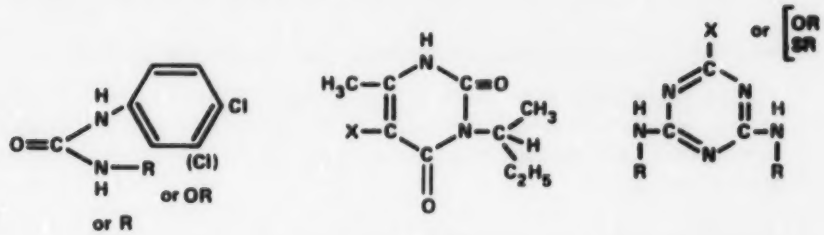
F. **DO NOT** administer aspirin or other antipyretics to control fever.

G. During convalescence, administer high-calorie, high-vitamin diet to facilitate repletion of body fat and carbohydrate stores.

H. Discourage subsequent contact with the toxicant for at least 4 weeks, to allow full restoration of normal metabolic processes.

UREA-, URACIL- AND TRIAZINE- BASED HERBICIDES

GENERAL CHEMICAL STRUCTURES



UREA DERIVATIVES | URACIL DERIVATIVES | s-TRIAZINE DERIVATIVES

X = HALOGEN R = ALKYL

COMMON COMMERCIAL PESTICIDE PRODUCTS

Urea derivatives: monuron (Monurex, Telvar), diuron (Di-on, Diurex, Karmex, Vonduron), linuron (HOE 2810, Afalon, Lorox, Sarclex).

Uracil derivatives: bromacil (Borea, Hyvar X, Hyvar X-L, Borocil IV, Urox HX or B, Isocil), terbacil (Sinbar).

Triazine derivatives: atrazine (Aatrex, Atranex, Gesaprin, Primatol A), simazine (Princep, Primatol S, Simanex, Gesatop), propazine (Milogard, Gesamil, Primatol P), prometone (Pramitol, Gesafram, prometon), atraton (Atratone), prometryn (Caparol, Gesagard, Primatol Q, Prometrex), ametryn (Evik, Ametrex, Gesapax), desmetryne (Semeron), terbutryn (Igran, Shortstop E), cyanazine (Bladex, Scogal), cyprazine (Outfox).

TOXICOLOGY

Adverse effects have occurred only rarely as a result of human contact with these herbicides. Most injuries reported have been skin irritation after prolonged contact. Improbability of severe systemic poisoning is indicated by LD_{50} values over 180 for all of the compounds listed under **COMMON COMMERCIAL PESTICIDE PRODUCTS.** In fact, LD_{50}'s for all but one herbicide are over 1,000; that for cyanazine is 182 mgm/kg.

Administered at very high dosage levels to laboratory animals and to sheep and cattle, some of these chemicals have been found to injure the nervous system, liver, and kidneys, and to cause increased permeability of capillaries. Anemia and altered adrenal function have also been detected in animals given extreme doses of certain triazine compounds. These effects have not been observed in persons exposed occupationally or by accidental ingestion.

In varying degree these herbicides are likely to produce irritation of the gut if ingested in substantial quantity. They are efficiently absorbed from the intestine, and presumably there is some absorption across the skin and lung. Following absorption, they are partially metabolized: native chemicals and metabolities are promptly excreted by the kidney and liver. In cases of accidental ingestion in humans, the hazards of petroleum distillate solvents may equal or exceed hazards presented by the active herbicidal ingredients.

POSSIBLE PRESENTING SYMPTOMS AND SIGNS OF INJURY

Some compounds of these classes cause **IRRITATION** of the eyes and mucous membranes, particularly if direct contact is protracted. **NAUSEA, VOMITING,** and **DIARRHEA** can be expected to result from ingestion of large quantities.

CONFIRMATION OF ABSORPTION

Certain industrial, university, and government laboratories can detect these compounds or their metabolites in the urine of persons who have absorbed significant amounts. These laboratories can be reached through health departments, poison control centers, or the U.S. Environmental Protection Agency.

TREATMENT

1. **FLUSH** contaminant from the eyes with copious amounts of clean water.
2. **WASH** chemical from the skin and hair with soap and water.
3. If one of these compounds has been **INGESTED,** optimal treatment will depend on dosage:
   A. Ingestions known to involve less than 10 mgm/kg body weight of the compounds having LD_{50} values over 1,000 (all except cyanazine) are probably managed best without induced emesis or gastric lavage, particularly if the ingestion occurred more than an hour prior to treatment. In these cases, administer 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to limit absorption. If a bowel movement does not occur in 4 hours, give **SODIUM SULFATE** as a cathartic (adults, 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg body weight in 1-6 ounces of water).
   B. In all other cases (unknown dosage, dosage over 10 mgm/kg body weight, and all cyanazine ingestions), **EMPTY THE STOMACH** either by induced **EMESIS** or by gastric **LAVAGE:**
      (1) If victim is alert and respiration is not depressed, give **SYRUP OF IPECAC** (adults, 12 years and older: 30 ml; children under 12: 15 ml).

CAUTION: **OBSERVE** the victim closely after administering **IPECAC.** If consciousness level declines, or if vomiting has not occurred in 15 minutes, proceed immediately to **INTUBATE, ASPIRATE,** and **LAVAGE** the stomach with isotonic saline or sodium bicarbonate solution.

Following emesis, have victim drink a suspension of 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to limit toxicant absorption.

(2) If victim is not fully alert or if respiration is depressed, empty the stomach immediately by **INTUBATION, ASPIRATION,** and **LAVAGE,** using isotonic saline or 5% sodium bicarbonate. Because these herbicides are usually dissolved in petroleum distillates, emesis and intubation of the stomach involve a serious **RISK** of chemical pneumonitis if solvent is aspirated. For this reason:

(a) If the victim is unconscious or obtunded, and if facilities are at hand, insert an **ENDOTRACHEAL TUBE** (cuffed, if available) prior to gastric intubation.

(b) Keep the victim's **HEAD BELOW THE LEVEL OF THE STOMACH** during intubation and lavage (Trendelenburg, or left lateral decubitus, with head end of table tipped downward). Keep the victim's head turned to the left.

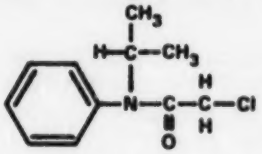
(c) **ASPIRATE PHARYNX** as regularly as possible to remove gagged or vomited stomach contents.

After aspiration of gastric contents and washing of stomach, instill 30 gm of **ACTIVATED CHARCOAL** in 3-4 ounces of water through a stomach tube to limit absorption of remaining toxicant. Do **NOT** instill milk, cream, or other substances containing vegetable or animal fats which may enhance toxicant absorption.

(3) If bowel movement has not occurred in 4 hours and if patient is fully conscious, give **SODIUM SULFATE** (Glauber's Salts) as a cathartic (adults, 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg body weight in 1-6 ounces of water).

ACETANILIDE-, ACETAMIDE-, CARBANILATE-, AND ANILIDE-, BASED HERBICIDES

CHEMICAL STRUCTURES



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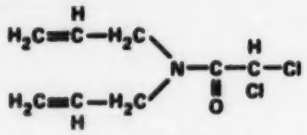

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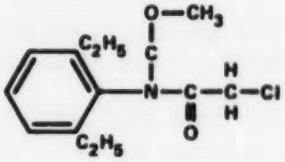

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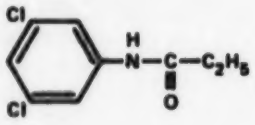

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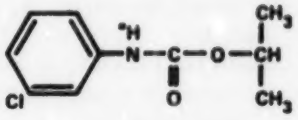

CHLORPROPHAM

COMMON COMMERCIAL PESTICIDE PRODUCTS

Propachlor (Ramrod), allidochlor (Randox, CDAA), alachlor (Lasso), chlorpropham (Chloro IPC, CIPC, Furloe), propanil (DPA, Stam, Propanex). Most technical formulations of these materials are in petroleum distillates.

TOXICOLOGY

These newer herbicides exhibit low systemic toxicity in laboratory rats (lowest oral LD_{50} of those listed is 700 mgm/kg). They are, however, irritating to skin, eyes, and mucous membranes. Propachlor and alachlor appear to have sensitizing properties. Severe skin reactions have occurred in sensitive individuals.

Any systemic toxicity of these compounds appears only at high dosage levels. Adverse effects from accidental ingestion by humans have not been reported. In all likelihood, substantial doses would cause gastrointestinal irritation.

SYMPTOMS AND SIGNS OF UNDUE EXPOSURE

IRRITATION of the skin and membranes of the upper respiratory tract is the principal adverse effect of contact with these compounds. Exaggerated reactions on repeated contact (**SENSITIZATION**) occur in some individuals. Propachlor has been the principal offender. Sensitization can result in **ACUTE** and **CHRONIC SKIN INJURY,** and in protracted irritation of the nose, eyes, and throat.

Nausea, abdominal distress, and diarrhea may be expected to result from ingestion of these compounds.

TREATMENT

1. **FLUSH** the chemical from the eyes with copious amounts of clean water. Severe contamination may require specialized ophthalmologic attention.
2. **WASH** contaminating herbicide from the skin and hair with soap and water. Severe irritation may require medical attention. Persons who become sensitized may need to take stringent precautions to avoid subsequent contact with these chemicals.
3. Ingestions known to involve less than 10 mgm/kg body weight are probably managed best without induced emesis or lavage, particularly if the ingestion **occurred more than an hour** before treatment. Administer 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to limit absorption. If a bowel movement has not occurred in 4 hours, give **SODIUM SULFATE** as a cathartic (adults, 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg body weight in 1-6 ounces of water).
4. Ingestions of more than 10 mgm/kg body weight, especially when ingestion occurred **less than an hour** before treatment, should be managed by prompt **EVACUATION** of the **STOMACH:**

   A. If victim is alert and respiration is not depressed, give **SYRUP** of **IPECAC** (adults, 12 years and older: 30 ml; children under 12: 15 ml).

      CAUTION: **OBSERVE** the victim closely after administering ipecac. If consciousness level declines or if vomiting has not occurred in 15 minutes, immediately **INTUBATE, ASPIRATE,** and **LAVAGE** the stomach with isotonic saline or sodium bicarbonate solution.

      Following emesis, have victim drink a suspension of 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to limit toxicant absorption.

   B. If victim is not fully alert, or if respiration is depressed, empty the stomach immediately by **INTUBATION, ASPIRATION,** and **LAVAGE,** using isotonic saline or 5% sodium bicarbonate. Because these herbicides are usually dissolved in petroleum distillates, emesis and intubation of the stomach involve a serious risk of

chemical pneumonitis if solvent is aspirated. For this reason:

(1) If the victim is unconscious or obtunded, and if facilities are at hand, insert an **ENDOTRACHEAL TUBE** (cuffed, if available) prior to gastric intubation.

(2) Keep the victim's **HEAD BELOW THE LEVEL OF THE STOMACH** during intubation and lavage (Trendelenburg, or left lateral decubitus; with head of table tipped downward). Keep the victim's head turned to the left.

(3) **ASPIRATE PHARYNX** as regularly as possible to remove gagged or vomited stomach contents.

After aspiration of gastric contents and washing of stomach, instill 30 gm of **ACTIVATED CHARCOAL** in 3-4 ounces of water through the stomach tube to limit absorption of remaining toxicant. Do not instill milk, cream, or other substances containing vegetable or animal fats which may enhance toxicant absorption.

C. If bowel movement has not occurred in 4 hours, and if patient is fully conscious, give **SODIUM SULFATE** (Glauber's Salts) as a cathartic (adult, 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg body weight in 1-6 ounces of water).

5. Severe sensitization reactions may require specialized medical management to control inflammatory responses that threaten to impair breathing or compromise circulation to the distal extremities. Reactions of this severity are rare.

DIMETHYLDITHIOCARBAMATE COMPOUNDS*

GENERAL CHEMICAL STRUCTURE

COMMON COMMERCIAL PESTICIDE PRODUCTS

Tetramethyl thiuram disulfide:
Thiram (Arasan, Thiramad, Thirasan, Thylate, Tirampa, Pomasol forte, TMTDS, Thiotex, Fernasan, Nomersan, Tersan, TUADS)

Metallodimethyldithiocarbamates:
Ziram, Pomasol Z forte (zinc), Ferbam (iron), Vapam (sodium).

TOXICOLOGY

Many compounds of this class are irritants and sensitizers. They may exacerbate allergic skin and respiratory disease, and sensitize otherwise normal individuals to subsequent contact with similar chemicals.

The two types of fungicide listed above are metabolized in a manner similar to disulfiram (tetraethyl thiuram disulfide) that is used to condition individuals against beverage alcohol. The molecule is first cleaved to yield two of alkyl dithiocarbamate, then further degraded to dialkyl amine and carbon disulfide. The metabolites are powerful inhibitors of multiple sulfhydryl enzymes in the liver and CNS. CS_2 is neurotoxic in its own right. To this extent, the toxicology of these fungicides probably resembles that of disulfiram, whose effects have been most thoroughly explored. Animal experiments indicate that thiram is more toxic than the medicinal disulfiram. Even so, systemic reactions (excluding irritation and sensitization) to the fungicides themselves have been rare.

The systemic toxicologic effects of these compounds fall into two categories: those following absorption of toxicant alone, and those resulting from ingestion of alcohol following absorption of a dithiocarbamate compound.

Given to laboratory animals in extreme doses, disulfiram itself causes gastrointestinal irritation, demyelinization of the central nervous system, and necrosis of the liver, spleen, and kidney parenchyma. Functional and anatomical CNS damage has been demonstrated in rats on high chronic dietary intakes of the iron and zinc dimethyldithiocarbamates. Peripheral

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* The ethylene bisdithiocarbamate fungicidal compounds are chemically similar to those considered here, but are metabolized in different ways and have somewhat different toxicologic properties.

neuropathy and psychotic reactions have occurred in alcohol-abstinent individuals on disulfiram regimens (ingestion of several hundred mgm daily). A possible role of the metabolite carbon disulfide has been suspected in these neurotoxic reactions.

Illness following combined intake of disulfiram and alcohol is due primarily to inhibition of liver enzymes necessary for oxidation of acetaldehyde to acetic acid. Peripheral vasodilation is the main pathophysiologic feature of the disulfiram-alcohol reaction, presumably due to high tissue levels of acetaldehyde. This may occasionally lead to shock, and even more rarely, to myocardial ischemia, cardiac arrhythmias, failure, and death. Animal experimentation has supported certain other biochemical mechanisms of toxicity involving reaction products of ethanol and disulfiram.

FREQUENT SYMPTOMS AND SIGNS OF INJURY AND POISONING BY DIALKYLDITHIOCARBAMATES

ITCHING, REDNESS, and **ECZEMATOID DERMATITIS** have resulted when sensitive or predisposed individuals come in contact with these compounds. Persons excessively exposed to air-borne fungicides have suffered **UPPER RESPIRATORY CONGESTION, HOARSENESS, COUGH,** and even **PNEUMONITIS.** When large amounts have been ingested, **NAUSEA, EMESIS,** and **DIARRHEA** ensue. **HYPOTHERMIA** and **ATAXIA** are characteristic. **MUSCLE WEAKNESS,** progressing to a condition of **ASCENDING PARALYSIS,** and finally **RESPIRATORY PARALYSIS,** can be anticipated from animal toxicologic studies based on extreme dosage.

The reaction to ethanol which follows absorption of disulfiram is characterized by **FLUSHING, SWEATING, POUNDING HEADACHE, SENSATION OF WARMTH, WEAKNESS, CONGESTION OF UPPER RESPIRATORY** and **CONJUNCTIVAL MEMBRANES, DYSPNEA, HYPERPNEA, CHEST PAIN, TACHYCARDIA, PALPITATION,** and **HYPOTENSION.**

Respiratory distress may resemble **ASTHMA,** and, in some instances, **RESPIRATORY DEPRESSION** has been life-threatening. **EMESIS** commonly occurs. Severe reactions may result in **SHOCK, UNCONSCIOUSNESS** and/or **CONVULSIONS,** and, therefore, threaten coronary insufficiency in predisposed individuals. Only under exceptional occupational circumstances can a person absorb enough of these fungicidal compounds to suffer a severe reaction to ethanol.

CONFIRMATION OF DIAGNOSIS

The native pesticides are so rapidly metabolized in the body that detection in blood or urine is rarely possible. There are biochemical methods for measuring blood acetaldehyde to confirm an ethanol-dithiocarbamate reaction.

TREATMENT

1. **WASH** contaminating fungicide from the skin and hair with soap and water. Atopic individuals and persons specifically sensitive to thiuram disulfide compounds (individuals recognized as "rubber-sensitive") should be permanently **REMOVED FROM CONTACT** with chemicals of this nature.
2. **FLUSH** contaminant from the eyes with fresh water for 10-15 minutes.
3. Treatment for **INGESTION OF DIMETHYLDITHIOCARBAMATE COMPOUNDS, NOT COMPLICATED BY ALCOHOL INGESTION:**

   A. If fungicidal compounds of this type have been **INGESTED,** it is first essential that the individual **NOT TAKE ANY FORM OF ALCOHOLIC BEVERAGE** for at least 3 weeks. (Gastrointestinal absorption of dialkyldithiocarbamates is protracted, and effects on critical enzymes are slowly reversible.)

   B. If vigorous emesis has not already occurred, and if victim is fully alert and respiration is normal, give **SYRUP OF IPECAC** to induce vomiting (adults, 12 years and older: 30 ml; children under 12: 15 ml).

      CAUTION: **OBSERVE** the victim closely **AFTER** administering **IPECAC.** If consciousness level declines, or if vomiting has not occurred in 15 minutes, proceed to empty the stomach by **INTUBATION, ASPIRATION** and **LAVAGE.**

      Following emesis, administer 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to bind toxicant remaining in the gut.

   C. If consciousness level or respiration is depressed, empty the stomach by **INTUBATION, ASPIRATION,** and **LAVAGE,** using all available means to avoid aspiration of vomitus: left lateral Trendelenburg position, frequent aspiration of the pharynx, and, in unconscious victims, tracheal intubation (using a cuffed tube) prior to gastric intubation.

      After aspiration of the stomach and washing with isotonic saline or sodium bicarbonate, instill 30 gm of **ACTIVATED CHARCOAL** in 3-4 ounces of water through the stomach tube to limit absorption of remaining toxicant.

   D. If the irritant properties of the toxicant fail to produce a bowel movement in 4 hours, and if the patient is fully conscious, give **SODIUM SULFATE** (Glauber's Salts) as a cathartic (adults, 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg of body weight in 1-6 ounces of water).

4. Treatment for a reaction to **ETHANOL INGESTION** following absorption of a **DIALKYLDITHIOCARBAMATE COMPOUND:**

   A. Administer 100% OXYGEN as long as the reaction continues. Oxygen usually gives substantial relief from the distressing symptoms and hypotension.

CAUTION: If respiration is depressed, administer oxygen by an intermittent positive pressure breathing device and observe the victim closely to maintain pulmonary ventilation artifically in case of apnea.

B. If the fungicide was **INGESTED** no more than 4 hours prior to treatment and vigorous emesis has not occurred, evacuate the stomach by **INTUBATION, ASPIRATION,** and **LAVAGE,** observing precautions cited in 3C, above.

C. Regardless of time interval since ingestion of fungicide, **ADMINISTER** 30 gm **ACTIVATED CHARCOAL** in 3-4 ounces of water to limit absorption of toxicant remaining in the gut. Absorption of the dithiocarbamate compounds is slow.

D. For adults and children over 12 years, inject 1.0 gm **ASCORBIC ACID** (Vitamin C) intravenously at a rate not exceeding 0.2 gm/minute. For children under 12, give 10-20 mgm per kg body weight. As a hydrogen-donor, ascorbic acid may have significant antidotal action against absorbed, but unreacted, dithiocarbamate compound.

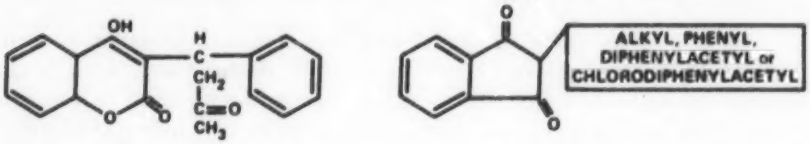
E. For severe or protracted reactions, **INFUSE** 5% **GLUCOSE** in D/W, or alternative glucose-containing fluids, to accelerate disposition of absorbed toxicants and metabolites.

F. Use sodium sulfate catharsis (3D above) only if no bowel movement occurs within 4 hours of the beginning of the reaction.

G. If the victim has suffered from arteriosclerosis, myocardial insufficiency, diabetes, neuropathy, cirrhosis, or other severe chronic disease, **OBSERVE** him **CAREFULLY** for 48 hours to insure that complications (especially myocardial infarction, toxic psychosis, and neuropathy) are treated promptly.

ANTICOAGULANT RODENTICIDES

STRUCTURES OF PRINCIPAL CLASSES



WARFARIN (COUMARIN-TYPE) 1,3-INDANDIONE TYPE

COMMON COMMERCIAL PESTICIDE PRODUCTS

Coumarin type: warfarin (Kypfarin, Warf-42, D-Con, Warficide, Prolin), coumafuryl (Fumarin), Dethmor, Rax.

1,3-indandione type: diphacinone, or diphenadione (Ramik), chlorophacinone (Drat, Caid, Liphadione, Microzul, Ramucide, Rotomet, Raviac, Topitox), pindone (Pivalyn, Pivacin, Tri-ban, Pival), valone, (PMP).

These materials are commonly added to baits or dissolved in small amounts of water for pest rodents to drink. One hundred grams of the prepared commercial baits must be ingested to yield 25 mgm of anticoagulant. Rodenticide "drinks" are made by adding dry concentrate (0.54 gm of active ingredient per 100 gm of powder) to specified volumes of water. The poison in the concentrate is coated on sugar or sand to facilitate measurement and handling.

TOXICOLOGY

Gastrointestinal absorption of these toxicants is efficient, beginning within minutes of ingestion and continuing for 2-3 days. Apparently, warfarin can also be absorbed across the skin, although the circumstances under which this has occurred are extraordinary.

Both types of anticoagulant depress the hepatic synthesis of substances essential to normal blood clotting: prothrombin (factor II), and factors VII, IX, and X. The anti-prothrombin effect is best known and provides the basis for detection and assessment of clinical poisoning. Direct damage to capillary permeability occurs concurrently. In rare instances, coumarin-type anticoagulants have caused ecchymosis and extensive skin necrosis in humans for reasons not related to excessive dosage.

Unlike the coumarin anticoagulants, the indandiones cause symptoms and signs of neurologic and cardiopulmonary injury in laboratory rats; these often lead to death before hemorrhage occurs. These actions may account for the somewhat greater toxicity of this class of anticoagulants. Cardiopulmonary and neurologic symptoms and signs have not been reported in human poisonings.

Lengthened prothrombin time from a toxic dose usually appears within 24

hours of toxicant ingestion and reaches a maximum in 36 to 72 hours. Without intervention, hypoprothrombinemia may persist 10-15 days, depending on the agent and dosage. Prothrombin depression will occur in response to doses that are much lower than those necessary to cause hemorrhage.

FREQUENT SYMPTOMS AND SIGNS OF POISONING

In most instances of accidental ingestion of anticoagulant baits, victims have remained asymptomatic, due to the small dosage taken. Even in cases involving ingestion of substantial doses, hypoprothrombinemia occurs without symptoms of poisoning. Hemorrhage appears only when extraordinary amounts have been absorbed. In these cases, the anticoagulants were either taken deliberately, were absorbed over long periods out of neglect of elementary hygienic standards, or were ingested by starving indigents who used quantities of rodent bait for food.

Victims of large doses exhibit **HEMATURIA, NOSEBLEED, HEMATOMATA, BLEEDING GUMS,** and **MELENA. ABDOMINAL PAIN** and **BACK PAIN** probably reflect hemorrhage in the abdominal and retroperitoneal tissues. **WEAKNESS** occurs as a result of **ANEMIA. RENAL COLIC** often complicates severe hematuria. Nasal and gastrointestinal hemorrhages have caused death from exsanguination.

CONFIRMATION OF DIAGNOSIS

Increase of the prothrombin time (Quick) reflects a reduction in serum prothrombin concentration, and occurs in response to physiologically significant absorption of these toxicants. This widely available clinical test offers a sensitive and reliable diagnostic method for detecting a toxic effect of these compounds. Readily detectable change in prothrombin time appears within 24-48 hours of ingesting the anticoagulant.

A few laboratories can measure warfarin and its metabolites in human urine, but it is rarely practical to use these determinations for diagnostic purposes.

TREATMENT

1. If it is known or suspected that anticoagulant rodenticide has been ingested recently, but that the total amount ingested was **LESS THAN 0.25 MGM/KG** body weight, administer a single dose of the specific antidote, **PHYTONADIONE, INTRAMUSCULARLY:** adults 12 years and older: 25 mgm IM; children under 12: 0.4 mgm/kg body weight IM.

   Note: **PHYTONADIONE** (Vitamin K_1, Mephyton, Aquamephyton, Konakion) specifically is required. Vitamin K_3 (menadione, Hykinone) and vitamin K_4 (menadiol) have little or no antidotal effect.

   This treatment is adequate when the total amount of toxicant ingested is known not to have exceeded the limits stated above, and in which no

pre-existing liver injury or blood clotting disease is present.

2. If the victim ingested anticoagulant rodenticide **WITHIN** the **PRECEDING 2-3 HOURS** in a quantity that may have exceeded 0.25 mgm/kg, **INDUCE VOMITING** with **SYRUP** of **IPECAC** (adults 12 years and older: 30 ml; children under 12: 15 ml). After emesis, give 30 gm **ACTIVATED CHARCOAL** in 4-6 ounces of water to limit absorption of rodenticide still in the gut.
3. If the victim may have ingested anticoagulant rodenticide any time within the preceding 15 days **IN AMOUNTS EXCEEDING** 0.25 mgm/kg, or if the victim may have a pre-existing liver or bleeding disease, determine the **PROTHROMBIN TIME.** Then administer **PHYTONADIONE INTRAMUSCULARLY** (adults, 12 years and older: 25 mgm; children under 12: 0.4 mgm/kg). Subsequent treatment will depend on the degree of prothrombin time lengthening, and on the estimated dosage and time of toxicant ingestion. High dosage or lengthening of the prothrombin time by more than 10 seconds over the control may dictate administration of a second dose of phytonadione (as above) and another measurement of prothrombin time 24 hours after the first. Reversal of prothrombin time usually occurs in 12-24 hours, but may require as long as three days.

   CAUTION: Doses of phytonadione in excess of 25 mgm are sometimes hepatotoxic, and should be given only when lower doses have not been effective. Doses in excess of 50 mgm involve significant hazard and are of doubtful benefit.

4. If the victim shows **SYMPTOMS** or **SIGNS** of **POISONING** (bleeding, anemia, hematomata) in addition to hypoprothrombinemia, it may be necessary to give **PHYTONADIONE INTRAVENOUSLY.** Aquamephyton may be administered by this route in doses of 25 mgm for adults, 12 years and older; or 0.4 mgm/kg for children under 12, repeating this amount once in 24 hours if bleeding continues. Inject at rates not exceeding 1 mgm/minute for adults, but proportionately slower in children. To achieve slow intravenous injection, dilute the phytonadione in either 0.9% saline or 5% glucose solution. Bleeding is usually controlled within 3-6 hours of intravenous infusion.

   CAUTION: Adverse reactions, some fatal, have occurred from intravenous phytonadione injections, even when recommended dosage limits and injection rates were observed. For this reason, the **INTRAVENOUS** route should be used **ONLY IN** cases of **SEVERE POISONING.** Flushing, dizziness, hypotension, dyspnea and cyanosis have characterized adverse reactions.

5. A. Antidotal therapy in cases of severe poisoning should be supplemented with **TRANSFUSIONS** of **FRESH BLOOD** or **FRESH FROZEN PLASMA.** Use of fresh blood or plasma represents the most rapidly effective method for stopping hemorrhage due to these

anticoagulants.

B. Determine **PROTHROMBIN TIMES** (and hemoglobin concentrations, if appropriate) every 6-12 hours to assess effectiveness of antidotal and antihemorrhagic measures.

C. When normal blood coagulability is restored, it may be advisable to drain large hematomata.

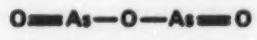
D. Ferrous sulfate therapy may be appropriate in the recuperative period to rebuild lost erythrocyte mass.

6. Give **ASCORBIC ACID** (vitamin C) orally or intramuscularly in mild and severe poisoning to limit capillary injury caused by the anticoagulants (adults, 12 years and older: 100 mgm; children under 12: 50-100 mgm).

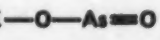
ARSENICAL PESTICIDES

CHEMICAL STRUCTURES

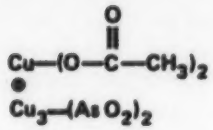
EXTREMELY TOXIC: (TRIVALENT INORGANIC ARSENICALS)



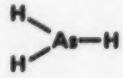
ARSENIC TRIOXIDE



POTASSIUM ARSENITE



COPPER ACETOARSENITE
(PARIS GREEN)

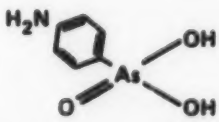


ARSINE (GAS)

MODERATELY TO HIGHLY TOXIC: (PENTAVALENT ORGANIC ARSENICALS)

MONO SODIUM
METHYL ARSONATE

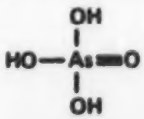
DI SODIUM
METHYL ARSONATE



ARSANILIC ACID

CACODYLIC ACID

(PENTAVALENT INORGANIC ARSENICAL)



ARSENIC ACID

COMMON COMMERCIAL PESTICIDE PRODUCTS

Inorganic arsenicals: arsenic trioxide (white arsenic), sodium arsenite (Acme Weed Killer, Atlas A, Penite, As-655 Weed Killer, Kill All), copper arsenite (Paris Green), copper ammonium arsenite (Chemonite), arsenic acid (Zotox Crabgrass Killer, Dessicant L-10, Lincks Liquid Di-met, Pax Total, Purina Top Grass and Weed Killer).

Organic arsenicals: MSMA (Ansar 170, Bueno, Weed-E-Rad, Ansar 529, Broadside, Crabgrass Dallis Grass Killer, Daconate, Fertilome Nutgrass and Weed Killer, Mad, Nutgrass Spray, Selector #1, Spot Grassy Weed Killer); DSMA (Ansar 8100, Biochecks, Bunee Crabgrass Killer, Chipco Crab Kleen, Clout, D Krab R + Prills, DMA, E Krab R, Greenfield Crabgrass and Dandelion Killer, Sears Liquid Crabgrass Killer, Lawn Weed Killer, Proturf Monocot Weed Control); cacodylic acid (Silvisar 510); sodium cacodylate (sodium dimethyl arsinate, Phytar 560, Acme Weed Killer); ammonium methane arsenate (AMA, Ansar 157, Super Crab E-Rad, C-4000, Antrol Crabgrass Killer, Crabgrass Broadleaf Killer, Systemic Crabgrass and Broadleaf Killer); methane arsonic acid (MAA, Ortho Crabgrass Killer).

TOXICOLOGY

Although the pentavalent arsenicals are generally less toxic than the inorganic trivalent chemicals, all poisonings by arsenic-containing substances should be regarded as serious threats to life and health. To some degree, the pentavalent compounds undergo reduction in the gut and/or body tissues to trivalent forms. Some absorption of solid arsenical compounds may occur by dermal or pulmonary routes, but the great majority of poisonings result from ingestion. Intestinal absorption is generally efficient. Most absorbed arsenic is excreted by way of the kidneys; a lesser proportion is excreted by the liver and gut. Arsine gas in absorbed rapidly by the lung; an arsenic metabolite is excreted in the urine.

Toxicology of arsine gas (absorbed by inhalation) is unique in that it causes hemolysis and secondary acute renal tubular necrosis. Arsine is not used as a pesticide, but is involved in the manufacture of organic arsenicals.

Trivalent arsenicals bind critical sulfhydryl-containing enzymes in tissues. When taken up from the gut, they injure the splanchnic vasculature, causing colic and diarrhea. Once absorbed, they produce toxic injury to the liver, kidney, bone marrow, brain and peripheral nerves. Liver injury is manifest as hepatomegaly, jaundice, and an increase in circulating hepatocellular enzymes LDH and GOT. Renal damage is reflected in albuminuria, hematuria, pyuria, cylindruria, then azotemia. Acute tubular necrosis may occur in severe poisoning. Injury to blood-forming tissues can take the form of agranulocytosis, aplastic anemia, thrombocytopenia, or pancytopenia. Toxic encephalopathy may become manifest as speech and behavioral disturbances. Peripheral neuropathy occurs in both acute and chronic forms. Inhalation of arsenic dusts may cause bronchitis or pneumonitis.

Sequelae of arsenic poisoning include cirrhosis, hypoplastic bone marrow, renal insufficiency, and peripheral neuropathy. Excessive exposures to arsenicals have caused cancers of skin and various epithelial tissues.

FREQUENT SYMPTOMS AND SIGNS OF POISONING

ACUTE arsenic poisoning (solid compounds):

COLIC, BURNING ABDOMINAL PAIN, VOMITING, and **WATERY** or **BLOODY DIARRHEA** are the primary manifestations of ingestion of solid arsenical poisons. Symptoms following ingestion of inorganic arsenicals are more severe than those resulting from ingestion of pentavalent organic arsenicals. Symptoms sometimes do not appear for minutes or even hours after ingestion. **HEADACHE, DIZZINESS, MUSCLE SPASMS, DELIRIUM,** and sometimes **CONVULSIONS** reflect direct injury to the central nervous system, as well as extracellular electrolyte disturbances and shock. **A GARLIC ODOR** to the breath and feces helps to identify the responsible toxicant. **SHOCK, TOXIC NEPHROSIS, HEPATITIS** (hepatomegaly and jaundice), and **NEUROLOGIC INJURY** (delirium, paralysis, respiratory depression) may progress to a fatal outcome.

SUBACUTE arsenic poisoning (solid compounds):

Dosages less than those necessary to produce severe acute symptoms are known to cause **CHRONIC HEADACHE, ABDOMINAL DISTRESS, SALIVATION, LOW-GRADE FEVER, AND PERSISTENT** symptoms of **UPPER RESPIRATORY IRRITATION.** Stomatitis and garlicky breath are characteristic.

CHRONIC arsenic poisoning (solid compounds):

Prolonged low intakes of arsenic cause **PERIPHERAL NEUROPATHY** (paresthesiae, pain, anesthesia, paresis, ataxia); **ENCEPHALOPATHY** (apathy); varied **DERMATOLOGIC DISORDERS** (keratoses, pigmentation, eczemas, brittle nails, loss of hair); and **TOXIC HEPATITIS** (hepatomegaly, sometimes progressing to cirrhosis with ascites). **WEAKNESS** and vulnerability to infections may result from bone marrow depression. Local **EDEMA,** frequently of the eyelids, characterizes some chronic poisoning cases.

ACUTE arsine poisoning (gas):

The gas causes **HEMOLYSIS** of red blood cells in addition to inhibition of cellular sulfhydryl respiratory enzymes. Hemolysis causes **HEMOGLOBINEMIA AND HEMOGLOBINURIA.** This in turn, causes **ACUTE TUBULAR NECROSIS.** Early symptoms of poisoning (chills, weakness, burning sensations) are followed by abdominal cramps, vomiting, and prostration, as renal function deteriorates to **ANURIA.**

CONFIRMATION OF DIAGNOSIS

Measurement of 24-hour urinary excretion of arsenic is probably the best way to confirm excessive arsenic absorption, although methods for blood arsenic concentration are available. Persons on ordinary diets usually excrete less than 20 μgm/day, but diets rich in seafood may generate as much as 200 μgm/day. Excretions above 100 μgm/day should be viewed with suspicion and tests should be repeated. Excretions above 200 μgm/day reflect

a potentially toxic intake.

The qualitative Gutzeit test for arsenic in the urine is available in most hospital laboratories, and is useful in identifying acute poisonings promptly.

Chronic storage of arsenic can be detected by analysis of hair or fingernails.

The hemoglobinuria caused by arsine is identified by finding the pigment in fresh urine from which intact red cells are absent.

TREATMENT FOR POISONING BY SOLID ARSENICALS

1. Flush contaminated **EYES, HAIR** and **SKIN** with copious amounts of fresh water.
2. In cases of poisoning by **RECENTLY INGESTED** (up to 6 hours) **ARSENICALS:**
   A. **INTUBATE** the stomach, **ASPIRATE,** and **LAVAGE** with 3 liters of isotonic saline or 5% sodium bicarbonate. Use all available precautions to avoid aspiration of vomitus:
      (1) If the victim is unconscious or obtunded, it is helpful to insert an **ENDOTRACHEAL TUBE** (cuffed, if available) prior to intubation.
      (2) Keep the victim's **HEAD BELOW THE LEVEL OF THE STOMACH** during intubation (Trendelenburg, or left lateral decubitus, with head of table tipped downward). Keep the victim's head turned toward the left.
      (3) **ASPIRATE** the pharynx as regularly as possible to remove gagged or vomited stomach contents.
   B. After lavage, **INSTILL** 60 gm **ACTIVATED CHARCOAL** in water: 6-8 ounces, or the smallest amount necessary to deliver the charcoal.
   C. If diarrhea or colic have not ensued within an hour of gastric lavage and charcoal administration, give **SODIUM SULFATE** as a cathartic (adults, 12 years and older: 15 gm in 6-8 ounces of water; children under 12: 0.2 gm/kg body weight in 1-6 ounces of water.
   D. Administer **INTRAVENOUS ELECTROLYTE** and **GLUCOSE** solutions to maintain hydration and to accelerate toxicant excretion. **COMBAT SHOCK** with **TRANSFUSIONS** of **WHOLE BLOOD,** and by inhalation of 100% **OXYGEN.**

      CAUTION: Monitor urine flow via catheter. Monitor fluid balance, body weight, and/or central venous pressure to guard against fluid overload resulting from acute tubular necrosis (anuria).

   E. **PROMPTLY** administer **DIMERCAPROL** (BAL, British antilewisite, dimercaptopropanol) **INTRAMUSCULARLY,** as the 10% solution in vegetable oil, to neutralize the toxic action of arsenicals. Recommended dosage schedule is:

	Mild Poisoning	Severe Poisoning
Days 1&2	2.5 mgm/kg q6h × 8 doses	3.0 mgm/kg q4h × 12 doses
Day 3	2.5 mgm/kg q12h × 2 doses	3.0 mgm/kg q6h × 4 doses
Succeeding 10 days	2.5 mgm/kg q24h × 10 doses	3.0 mgm/kg q12h × 20 doses

CAUTION: **DIMERCAPROL** can cause troublesome side effects (hypertension, tachycardia, nausea, headache, paresthesiae and pain, lachrimation, sweating, anxiety, and restlessness). Although usually not so severe as to handicap treatment, these manifestations may require antihistaminic therapy for adequate control.

F. Intense abdominal pain may require morphine (adults, 12 years and older: 4-15 mgm; children under 12: 0.1–0.2 mgm/kg.)

G. Severe poisoning (especially when renal function is impaired) may require hemodialysis to remove arsenic combined with dimercaprol from the blood.

3. If arsenical was ingested more than 48 hours prior to treatment, or if excessive absorption has occurred over an extended period, treatment should probably be limited to administration of dimercaprol as prescribed in 2E plus nutritional supplements to restore metabolic functions as promptly as possible.

TREATMENT FOR POISONING BY ARSINE GAS

1. **REMOVE** the victim to **FRESH AIR.**
2. **MAINTAIN RESPIRATION** and **CIRCULATION** by resuscitation and cardiac massage, if necessary.
3. Administer **INTRAVENOUS FLUIDS** as promptly as possible to dilute hemoglobin in the glomerular filtrate and minimize tubular injury. Use enough sodium bicarbonate to keep the urine alkaline.

   CAUTION: Monitor urine flow via catheter. Monitor fluid balance, body weight, and/or central venous pressure to guard against fluid overload resulting from acute tubular necrosis.
4. Administer **DIMERCAPROL** as recommended in 2E even though it has only limited effect in arsine poisoning.
5. **EXCHANGE BLOOD TRANSFUSIONS** and **PERITONEAL DIALYSIS** have saved the lives of victims of arsine poisoning suffering acute tubular necrosis.

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